

REMARKS

Claims 1-45 are canceled. Claims 46-74 have been added, and are therefore pending in the present application. New claims 46-67 are supported by original Claim 5 and page 8, lines 5-20 of the specification. Claim 46 recites variants of a *Myceliophthora thermophila* laccase wherein said variant consists of between 1 and 14 modifications. It is respectfully submitted that the present amendment presents no new issues or new matter and places this case in condition for allowance. Reconsideration of the application in view of the above amendments and the following remarks is requested.

I. The Rejection of Claims 16, 19, 20 and 39-42 under 35 U.S.C. 112 (Written Description)

Claims 16, 19, 20 and 39-42 are rejected under 35 U.S.C. 112, paragraph 1, as lacking written description support. The Examiner states that in order "to fully describe a genus of genetic material,...applicants must (1) fully describe at least one species of the claimed genus sufficient to represent said genus where a skilled artisan, in view of the prior art, could predict the structure of other species encompassed by the genus claim and (2) identify the common characteristics of the claimed molecule, e.g., structure, physical and/or chemical characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or a combination of these." February 24, 2005 Office Action at Page 6. The Examiner rejects the claims on the grounds that "the specification fails to define those structural features that are commonly possessed by members of the genus that distinguish them from other members of the genus of laccases." February 24, 2005 Office Action at Pages 6-7. In connection with these grounds for rejection, the Examiner further notes that "the specification does not teach the correlation between structure and function common to all members of said genus." February 24, 2005 Office Action at Page 7. The Examiner concludes that "one skilled in the art cannot visualize or recognize the identity of the members of the genus." *Id.*

New Claims 46-67 have been added. Claims 46-67 are directed to laccase variants (and various composition and methods of using the laccase variants) which have a very high structural similarity to a *Myceliophthora thermophila* laccase, as the claims recite that the variant consists of between 1 and 14 modifications in the *Myceliophthora thermophila* laccase. The claims also recite that the variant has at least one substitution at a position corresponding to at least one of the following positions in SEQ. ID NO. 10: V52; G121; F141; H206; P336; T365; I380; I382; V406; A506; or W507. In addition to these modifications, other modifications are described in the

specification or known in the art, including, for example, as described in Svendsen et al. (WO 98/38286) and Pederson et al. (U.S. Patent No. 5,925,554).

In addition, the specification also provides detailed guidance for identifying other modifications which can be made, such as, for example, using the three-dimensional structure (atomic coordinants of Appendix 1) to identify suitable amino acids for modifications. In particular, the specification discloses the three dimensional structure of a *Coprinus* laccase. See Page 3 at line 20-29 and Appendix 1. This three-dimensional structure is stated to be representative for the structure of any *Coprinus*-like laccase, see Page 3, lines 22-23; see also Page 4, lines 15-29, including *Myceliophthora thermophila* laccase. The specification further discloses specific methods for designing *Myceliophthora thermophila* laccase variants using the three-dimensional structure of a *Coprinus* laccase, as a guide to determining parts of the *Coprinus*-like laccase (including, a *Myceliophthora thermophila* laccase) relevant to the stability of the laccase. See, for example, Page 5, lines 10-25.

Thus, the specification provides a written description sufficient for the artisan to conclude that Applicants were in possession of a variant of a *Myceliophthora thermophila* laccase consisting of between 1 and 14 modifications, wherein at least one of the modifications is a substitution at a position corresponding to at least one of the following positions in SEQ. ID NO:10: V52; G121; F141; H206; P336; T365; I380; I382; V406; A506; or W507, provided that wherein the substitution is at a position corresponding to position A506, the substitution is A506C, F, G, H, I, K, L, M, N, P, Q, R, S, T, V, or Y in SEQ ID NO: 10, and wherein the variant has laccase activity.

For the foregoing reasons, Applicants submit that the claims overcome this rejection under 35 U.S.C. 112. Applicants respectfully request reconsideration and withdrawal of the rejection.

II. The Rejection of Claims 16, 19, 20 and 39-42 under 35 U.S.C. 112 (Enablement)

The Examiner further rejects Claims 16, 19, 20 and 39-42 under 35 U.S.C. 112, paragraph 1, as lacking enablement. The Examiner alleges that "the specification, while being enabling for a variant of a *Myceliophthora thermophila* having an amino acid sequence that differs from SEQ ID No:10 by a mutation corresponding to at least one of the specific positions therein, does not reasonably provide enablement for a variant of *Myceliophthora thermophila* laccase having an amino acid sequence that comprises a substitution corresponding to at least one of the 11 specific positions wherein said variant amino acid sequence has an amino acid sequence at least 60% homologous with Seq. ID No:1." February 24, 2005 Office Action at Page 7. The Examiner concludes that the specification does not enable one skilled in the art "to make the

invention commensurate in scope with these claims." Id. Specifically, the Examiner states that the specification is deficient in this respect because it fails to provide sufficient guidance as to (A) which regions of the protein may be modified without effecting laccase activity; (B) the general tolerance of laccases to modification and the extent of such tolerance; (C) a rational and predictable scheme for modifying laccase residues with an expectation of retaining the desired biological function; and (D) which of the "essentially infinite choices available" is likely to be successful. February 24, 2005 Office Action at Pages 9-10. This rejection is respectfully traversed.

Claims 46-67 have been added. Applicants respectfully submit that claims 46-67 are enabled. Claims 46-67 are directed to laccase variants (and various compositions and methods of using the laccase variants) which have a very high structural similarity to a *Myceliophthora thermophila* laccase, as the claims recite that the variant consists of between 1 and 14 modifications in the *Myceliophthora thermophila* laccase. The claims also recite that the variant has at least one substitution at a position corresponding to at least one of the following positions in SEQ. ID No. 10: V52; G121; F141; H206; P336; T365; I380; I382; V406; A506; or W507. It would be routine for the skilled artisan to make the claimed variants commensurate in scope with the claims. Using, for example, the *Myceliophthora thermophila* laccase amino acid backbone of SEQ ID NO:1, an artisan could readily produce variants having between 1 and 14 modifications, including, having at least one substitution of an amino acid corresponding to amino acid residues V52; G121; F141; H206; P336; T365; I380; I382; V406; A506; or W507 in SEQ ID NO:10.

In addition, the specification describes laccases modified at other positions. See, for example, page 6 at line 25-page 7 at line 4; Page 8, lines 5-20. Modifications at other positions are also well known in the art. See, for example, Svendsen et al. (WO 98/38286) and Pederson et al. (U.S. Patent No. 5,925,554). Based on Applicants' disclosure, the skilled artisan would be sufficiently guided as how to make other modifications in addition to the modifications recited in the claims to obtain the benefit of the invention.

Applicants also note that the specification discloses the three dimensional structure of a *Coprinus* laccase. See Page 3 at line 20-29 and Appendix 1. The structural coordinates for the solved crystal structure are provided in Appendix 1. See Page 3, lines 26-29 and Appendix 1. This three-dimensional structure is stated to be representative for the structure of the *Coprinus*-like laccase family, see Page 3, lines 22-23; see also Page 4, lines 15-29, including *Myceliophthora thermophila* laccase. The specification further discloses specific methods for designing laccase variants using this three-dimensional structure.

Thus, it is respectfully submitted that the claims are enabled. For the foregoing reasons, Applicants submit that the claims overcome this rejection under 35 U.S.C. 112. Applicants respectfully request reconsideration and withdrawal of the rejection.

III. The Rejection of Claims 16, 19 , 20 and 39-42 under 35 U.S.C. 112

Claims 16, 19 , 20 and 39-42 are rejected under 35 U.S.C. 112, Paragraph 2 as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. February 24, 2005 Office Action at Page 10. Specifically the Examiner notes that while "the claims recite the % homology," id., "the percent homology can be calculated using different algorithms and parameters." Id. "Without knowing such data," the Examiner adds, "it is impossible to know which sequences are encompassed by the claim." Id. This rejection is respectfully traversed.

The calculation of percent homology is routine in the art. The specification, e.g., fully describes methods of calculating % homology by using the UWGCG program using the GAP program with default parameters (identified in the specification). See Page 2, lines 9-31. Thus, the skilled artisan would be able to calculate the % homology and know which sequences are encompassed by the claims.

For the foregoing reasons, Applicants submit that the claims overcome this rejection under 35 U.S.C. 112. Applicants respectfully request reconsideration and withdrawal of the rejection.

IV. The Rejection of Claim 40 under 35 U.S.C. 112

Claim 40 (now Claim 69) is rejected under 35 U.S.C. 112, Paragraph 2. Specifically, the Examiner states that Claim 40 is unclear as reciting the term "protected enzymes" because the specification does not define the term. February 24, 2005 Office Action at Page 11. This rejection is respectfully traversed.

The specification states that protected enzymes may be prepared according to the methods disclosed in EP 238,216. Page 1, lines 10-11. Thus the specification discloses the meaning of the term "protected proteins" in sufficient detail to satisfy the requirements of Paragraph 2 of 35 U.S.C. 112, as an artisan would readily understand what this term means, such as, for example, as is described in EP 238,216. For the foregoing reasons, Applicants submit that the claims overcome this rejection under 35 U.S.C. 112. Applicants respectfully request reconsideration and withdrawal of the rejection.

V. The Rejection of Claims 16 and 39-42 under 35 U.S.C. 103

Claims 16 and 39-42 are rejected under 35 U.S.C. 103 as being unpatentable in view of Svendsen et al. This rejection is respectfully traversed.

Svendsen et al. disclose the A506E substitution. Applicants respectfully submit that the new claims render the rejection over Svendsen et al. moot.


For the foregoing reasons, Applicants submit that the claims overcome this rejection under 35 U.S.C. 103. Applicants respectfully request reconsideration and withdrawal of the rejection.

VI. Conclusion

In view of the above, it is respectfully submitted that all claims are in condition for allowance. Early action to that end is respectfully requested. The Examiner is hereby invited to contact the undersigned by telephone if there are any questions concerning this amendment or application.

Respectfully submitted,

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